Caspofungin - Concluding Comments

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Caspofungin - Major Conclusions

- New class of antifungal agents
- Novel mechanism of action
- Clear efficacy in salvage *Aspergillus* infection
  - Disease with high mortality
  - Population with limited therapeutic options
- Very favorable safety profile

Issues for Consideration

- Antimicrobial activity of caspofungin against *Aspergillus* spp.
- Distribution and metabolism of caspofungin
- Size of efficacy database for aspergillosis

Characterization of Antimicrobial Activity

- Clear in vitro effect of caspofungin across *Candida* and *Aspergillus* spp.
  - In vitro *Aspergillus* observations not consistent with classical definitions of fungicidal or fungistatic agent
  - Effects consistent with mechanism of action
- Results from in vivo models demonstrate sustained antifungal activity similar to amphotericin
- Clear clinical responses in highly immunocompromised patients

Caspofungin Distribution and Metabolism

- Pharmacokinetics well defined across range of patient populations
- Drug interactions evaluated by Phase I studies and extensive population PK
  - Combined approach provides evaluation of many drug combinations
  - Few situations appear to require dose modifications
- Clear, simple dosing guidelines can be provided

Size of Aspergillosis Efficacy Database

- Uncommon patient population with high mortality
- Utilized non-comparative trial using strict criteria and expert panel review
- Clarity of efficacy data balances limited patient numbers
  - Certainty of diagnosis and response
  - Consistency of clinical response
  - Additional evidence continues to support favorable response rate

Summary

- Less typical aspects of caspofungin program have been carefully reviewed throughout development
- Quality and consistency of data provides clear demonstration of clinical efficacy
- Safety profile very favorable and offers important clinical utility
- Caspofungin represents an important therapeutic option for a patient population with a very poor prognosis

CANCIDAS® is indicated for the treatment of invasive aspergillosis in patients who are refractory to or intolerant of other therapies.